Support for new claims 20 and 21 can be found in the originally-filed specification of 09/251,835 at page 23, lines 27-29; and page 24, lines 1-2.

Support for new claim 22 can be found in the originally-filed specification of 09/251,835 at page 22, lines 1-3.

Support for new claim 23 can be found in the originally-filed specification of 09/038,261 at page 13, lines 9-15.

Support for new claim 24 can be found in the originally-filed specification of 09/038,261 at page 10, lines 19-24; page 13, lines 17-21.

Support for new claim 25 can be found in the originally-filed specification of 09/203,939 at page 22, lines 17-18; page 23, lines 16-17.

Support for new claim 26 can be found in the originally-filed specification of 09/203,939 at page 23, lines 16-24.

Support for new claim 27 can be found in the originally-filed specification of 09/038,261 at page 14, line 4.

Support for new claim 28 can be found in the originally-filed specification of 09/359,326 at page 31, lines 7-8.

Support for new claim 29 can be found in the originally-filed specification of 09/203,939 at page 23, lines 16-24.

Support for new claim 30 can be found in the originally-filed specification of 09/203,939 at page 23, lines 16-24. Support can also be found in the originally-filed specification of 09/359,326 at page 31, lines 1-7.

Support for new claim 31 can be found in the originally-filed specification of 09/038,261 at page 13, lines 33-36; and page 14, lines 1-6.

Support for new claim 32 can be found in the originally-filed specification of 09/038,261 at page 14, line 4.

Support for new claim 33 can be found in the originally-filed specification of 09/359,326 at page 31, lines 7-8.

Support for new claims 34 and 35 can be found in the originally-filed specification of 09/038,261 at page 13, lines 33-36; and page 14, lines 1-6. Support can also be found in the originally-filed specification of 09/359,326 at page 31, lines 1-7.

Support for amended claims 1-3 and new claims 18-35 are found in the specification as originally filed and therefore do not involve new matter. Entry of these claims is respectfully requested.

Objection to the Drawings:

In paragraph 5 of the Office Action, the Patent Office issued an objection to the drawings. Applicants will attend to this matter in the future.

Amendment of the Title:

In paragraph 6 of the Office Action, the Patent Office is requesting a more descriptive title. In response, applicants provide an amended title herein. The amendment of the title does not involve new matter. Entry of the amendment is requested.

Amendment of the Brief Description of The Drawings:

In paragraph 6 of the Office Action, the Patent Office objected the Brief Description of the Drawings because they did not provide separate descriptions for each view of the figures. Accordingly, applicants provide amended Brief Description of the Drawings herein. The amendments of the Brief Descriptions of the Drawings now include separate descriptions of the following Figures: 1, 7, 8, 9, 10, 11, 12, 14, 15, 16, 39, 40, and 47. The amendments of the Brief Descriptions of the Drawings do not involve new matter. Entry of the amendments is requested.

Amendment of the Specification:

In paragraph 6 of the Office Action, the Patent Office objected the specification at page 24 because it did not include the current address of the American Type Culture Collection (ATCC). Accordingly, applicants amended the specification herein; page 24 is amended to include the current address of ATCC. The amendment of the specification at page 24 does not involve new matter. Entry of the amendments is requested.

Additionally, applicants provide amendments of the specification at page 1, line 7. The amendment corrects a typographical error and does not involve new matter. Entry of the amendment is requested.

Applicants also provide amendments of the specification to include the sequence identification number indicators (e.g., SEQ ID NO:). Amendments of the specification includes the following: page 6, line 6; page 6, lines 8-12; page 18, lines 1-3; page 18, lines 12-13; page 18, lines 13-15; page 18, lines 22-23; page 19, line 12; page 19, lines 16-17; page 19, lines 28-29; page 20, lines 4-5; page 32, lines 21-22; page 32, lines 22-23; page 39, lines 20-21; page 74, lines 7-9; page 74, lines 17-19; page 79, lines 22-23; page 81, lines 12-14; page 97, line 7; page 104, line 24; page 104, line 25; page 106, lines 18-19; and page 118, lines 31-32. These amendments do not involve new matter. Entry of these amendments is requested.

The amendment at page 11, lines 19-24 removes the brief description of Figure 37B and does not involve new matter. Entry of the amendment is requested.

The amendment at page 15, lines 21-22, corrects a typographical error and does not involve new matter. Entry of the amendment is requested.

The amendment at page 15, lines 24-25, corrects a typographical error and does not involve new matter. Entry of the amendment is requested.

The amendment at page 15, lines 27-28, corrects a typographical error and does not involve new matter. Entry of the amendment is requested.

Amendment of the Abstract:

In paragraph 6 of the Office Action, the Patent Office objected the description in the Abstract because it does not refer to the claimed antibodies. Applicants provide amended Abstract herein. The amendment of the abstract now provides a description of the claimed anti-PSCA antibodies.

Support for the amendment to the Abstract can be found in the originally-filed application, at page 16, lines 23-26; page 22, lines 23-25; page 25, lines 1-5; page 25, lines 25-30; page 26, lines 1-10; page 26, lines 20-22; page 28, lines 20-29; page 29, lines 5-9; page 30, lines 28-30; page 31, lines 1-12. The amendment to the Abstract does not involve new matter. Entry of the amendment is requested.

Providing Copies of the References in the Information Disclosure Statement (IDS):

In paragraph 7 of the Office Action, as requested by the Patent Office, applicants provide a copy of each of the IDS references 1-112 herein. The copies of the references are attached as Exhibits 1-112.

APPLICANTS' INVENTION:

The present invention provides antibodies which recognize and bind a *specific* portion of the Prostate Stem Cell Antigen (PSCA) protein. Embodiments of the invention include antibodies which recognize and bind the N-terminal portion (e.g, part or all of amino acids 2-50), or bind the middle portion (e.g., part or all of amino acids 46-109), or bind the C-terminal portion (e.g., part or all of amino acids 85-123) of the PSCA protein. Other embodiments of the invention include anti-PSCA antibodies which are: chimeric antibodies; human antibodies; internalizing antibodies; fragments of anti-PSCA antibodies; recombinant proteins including the antigen binding region the anti-PSCA antibodies; immunotoxins; and immunoconjugates. The present invention also provides hybridomas which produce the antibodies of the invention.

The antibodies of the present invention are distinguishable from the antibodies disclosed in Au-Young. The present invention provides anti-PSCA antibodies which bind to *specific* portions of the PSCA protein, such as amino acids 2-50, 46-109, or 85-123, as described in SEQ ID NO:2.

OBJECTIONS TO THE CLAIMS:

In paragraph 8 of the Office Action, the Patent Office objected to pending claim 3, because it did not recite that residues 85-123 are described in "SEQ ID NO:2". Applicants amend claim 3 to recite that residues 85-123 are in SEQ ID NO:2. The amendment to claim 3 does not involve new matter. Entry of the amendment is requested.

In paragraph 8 of the Office Action, the Patent Office objected to pending claim 12, because it is dependent upon canceled claim 8. Applicants cancel claim 12 without prejudice herein.

THE REJECTION UNDER §112, SECOND PARAGRAPH:

In paragraph 10b, the Patent Office rejects claim 4 under 35 U.S.C. §112, second paragraph. The Patent Office alleges that claim 4 is indefinite because there is insufficient antecedent basis for the limitation "internalized by the cell". Furthermore, the Patent Office alleges that claim 4 does not make it clear which cell is internalized. Applicants have cancelled claim 4, without prejudice, and thus the rejection is moot.

In paragraph 10a, the Patent Office rejects claim 5 under 35 U.S.C. §112, second paragraph. The Patent Office the Patent Office alleges that claim 5 is indefinite because the meaning of the phrase "murine antigen binding region residues and human antibody residues" is not clear. Applicants have cancelled claim 5, without prejudice, and thus the rejection is moot.

COPIES OF PRIOR PATENT APPLICATIONS:

In paragraph 11 of the Office Action, the Patent Office requests that applicants provide copies of patent applications 09/318,503, 09/251,835, and 09/203,939, because these applications are allowed cases and are presently unavailable for the Patent Office's inspection. Applicants provide a copy of each of these applications herein, attached as Exhibit #113-115, respectively.

PRIORITY DATES GRANTED TO APPLICANTS' CLAIMS:

The priority of the subject application is as follows. The subject application is a continuation-in-part (CIP) of U.S. Serial No. 09/318,503, filed May 25, 1999, which is a CIP of U.S. Serial No. 09/251,835, filed February 17, 1999, which is a continuation-in-part (CIP) of U.S. Serial No. 09/203,939, filed December 2, 1998, which is a CIP of U.S. Serial No. 09/038,261, filed March 10, 1998; claiming the priority of provisional applications, U.S. Serial No. 60/228,816, filed March 10, 1997; U. S. Serial No. 60/071,141 filed January 12, 1998 and; U. S. Serial No. 60/074,675, filed February 13, 1998. This application further claims the benefit of the filing dates

of U.S. Serial Nos. 60/124,658 filed March 16, 1999; 60/120,536 filed February 17, 1999; and 60/113,230 filed December 21, 1998.

Priority Date of Claims 1, 3, 12, 16, and 17:

New claim 31 generally corresponds to claims 12, 16, and 17. Therefore, applicants contend that the priority date for new claim 31 is March 10, 1998 for the reasons discussed above.

Priority Date of Claims 2, 9-11, and 15:

The Patent Office granted the priority date of December 21, 1998, for claims 2, 9-11, and 15, based on the disclosure of U.S. Serial No. 60/113,230. Applicants respectfully disagree with the priority date the Patent Office has granted for claims 2, 9-11, and 15.

Claim 2 recites monoclonal antibodies which bind the middle portion of PSCA. Support for anti-PSCA antibodies which bind a portion of PSCA, such as the middle portion, can be found in U.S. Serial No. 09/038,261, filed March 10, 1998 at the following pages: page 10 lines 13-14; page 11, lines 14-15, and lines 22-23. Therefore, applicants contend that claim 2 should be granted the priority date of March 10, 1998. Applicants request that the Patent Office grant claim 2 the priority date of March 10, 1998.

New claim 23 generally corresponds to claim 9. New claim 23 recites hybridomas which produce monoclonal antibodies that bind the N-, middle, or C-terminal portions of PSCA. Specific hybridomas which produce anti-PSCA antibodies that bind the N-, middle, or C-terminal portions of PSCA were deposited with the American Type Culture Collection on December 11, 1998, in connection with U.S. Serial No. 09/203,939, filed December 2, 1998. Therefore, applicants contend that claim new 23 should be granted the priority date of December 2, 1998. Applicants request that the Patent Office grant claim 23 the priority date of December 2, 1998.

New claim 25 generally corresponds to claim 10. New claim 25 recites a recombinant protein comprising the antigen-binding region of an anti-PSCA monoclonal antibody. Support for claim 25 can be found in U.S. Serial No. 09/203,939, filed December 2, 1998 at the following pages: page 22, lines 16-18; and page 23, lines 16-19. Therefore, applicants contend that new claim 25 should be granted the priority date of December 2, 1998. Applicants request that the Patent Office grant claim 25 the priority date of December 2, 1998.

New claim 24 generally corresponds to claim 11. New claim 24 recites antibody fragments which bind the N-, middle, or C-terminal portions of PSCA. Support for antibody fragments which bind to a portion of PSCA can be found in U.S. Serial No. 09/038,261, filed March 10, 1998 at the following pages: page 10 lines 13-14; page 11, lines 14-15, and lines 22-23. Also, support can be found at page 13, lines 18-21. Therefore, applicants contend that new claim 24 should be granted the priority date of March 10, 1998. Applicants request that the Patent Office grant claim 24 the priority date of March 10, 1998.

New claim 29 generally corresponds to claim 16 and new claims 26, 27, and 28 generally correspond to claims 15, 19, and 21, respectively. New claim 29 recites an immunotoxin comprising a recombinant protein having an antigen-binding region of an anti-PSCA antibody conjugated with a cytotoxic agent. Support for claim 29 can be found in U.S. Serial No. 09/203,939, filed December 2, 1998 at the following pages: page 22, lines 6-18, and page 23, lines 16-19. Applicants request that the Patent Office grant new claims 26-29 the priority date of December 2, 1998.

Priority Date of Claims 4-6 and 13-14:

The Patent Office granted the priority date of July 20, 1999, for claims 4-6 and 13-14, based on the disclosure of the subject application (e.g., U.S. Serial No. 09/359,326). However, these claims are entitled to an earlier priority date. The Patent Office is in error.

New claim 22 generally corresponds to claim 4. New claim 22 recites internalizing antibodies, which are disclosed in U.S. Serial No. 09/251,835, filed February 17, 1999. Support for internalizing antibodies can be found in the '835 application at page 22, lines 1-3. Therefore, applicants contend that new claim 22 should be granted the priority date of February 17, 1999. Applicants request that the Patent Office grant claim 22 the priority date of February 17, 1999.

New claim 19 generally corresponds to claim 5. New claim 19 recites anti-PSCA antibodies comprising a murine immunoglobulin variable region and a human immunoglobulin constant region, which are disclosed in U.S. Serial No. 09/038,261, filed March 10, 1998. Support for these antibodies can be found in the '261 application at page 13, lines 29-31. Therefore, applicants contend that new claim 19 should be granted the priority date of March 10, 1998. Applicants request that the Patent Office grant claim 19 the priority date of March 10, 1998.

New claim 20 generally corresponds to claim 6. New claim 20 recites anti-PSCA antibodies which are human antibodies, which are disclosed in U.S. Serial No. 09/251,835, filed February 17, 1999. Support for these antibodies can be found in the '835 application at page 23, lines 27-29; and page 24, lines 1-2. Therefore, applicants contend that new claim 20 should be granted the priority date of February 17, 1999. Applicants request that the Patent Office grant claim 20 the priority date of February 17, 1999.

NO HUMANIZED NOT HUMAN

New claims 31 and 34 generally correspond to claim 13. New claim 31 recites an immunoconjugate comprising an anti-PSCA antibody conjugated with a therapeutic agent, which is disclosed in U.S. Serial No. 09/038,261, filed March 10, 1998. New claim 34 recites an immunoconjugate comprising an anti-PSCA antibody conjugated with a cytotoxic agent, which is disclosed in U.S. Serial No. 09/038,261, filed March 10, 1998. Support for antibodies conjugated to a cytotoxic agent can be found at page 13, lines 33-36; and page 14, lines 1-4. Therefore, applicants contend that claim 34 should be granted the priority date of March 10, 1998. Applicants request that the Patent Office grant claim 34 the priority date of March 10, 1998.

New claim 34 replaces claim 14. New claim 34 recites an immunoconjugate comprising an anti-PSCA antibody conjugates with a cytotoxic agent, which is disclosed in U.S. Serial No. 09/038,261, filed March 10, 1998. Support for antibodies conjugated to a cytotoxic agent can be found at page 13, lines 33-36; and page 14, lines 1-4. Therefore, applicants contend that claim 34 should be granted the priority date of March 10, 1998. Applicants request that the Patent Office grant claim 34 the priority date of March 10, 1998.

OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTIONS

In paragraph 13 of the Office Action, the Patent Office provisionally rejected claims 1-3 and 9 under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 2 and 12-13 of co-pending application U. S. Serial No. 09/203,939, filed December 2, 1998.

Upon an indication of allowability from the Patent Office, applicants will provide a terminal disclaimer.

THE REJECTIONS UNDER 35 U.S.C. §102(b):

In paragraph 15 of the Office Action, the Patent Office rejected pending claims 1-5 and 9-11 under §102(b) as allegedly anticipated by Au-Young (U.S. Patent 5,856,136). The Patent Office alleges that Au-Young produced antibodies that are directed to the same amino acid sequences as recited in the claimed invention. The Patent Office also alleges that Au-Young teaches antibodies, which are identical to the antibodies of the invention.

Applicants traverse the rejection. Applicants respectfully contend that the Patent Office improperly rejected claims 1-5 and 9-11 under 35 U.S.C. §102(b).

Applicants respectfully traverse the §102(b) rejection. Au-Young does not disclose each and every element of the claimed invention in a manner sufficient to enable one skilled in the art to reduce the antibodies of the invention to practice.

The Standard For Novelty

A claimed invention is anticipated if each and every element of the claimed invention is disclosed in a single prior art reference in a manner sufficient to enable one skilled in the art to reduce the invention to practice, thus placing the invention in possession of the public. W.L. Gore & Assocs., Inc. v. Garlock, Inc., 220 U.S.P.Q. 303 (Fed. Cir. 1983), *cert. Denied* 469 U.S. 851 (1984); In re Donohue, 226 U.S.P.Q. 619 (Fed. Cir. 1985); Scripps Clinic & Research Found. V. Genentech, Inc., 927 F. 2d 1565, 1576-7 (Fed. Cir.), clarified, on recons., 1991 U.S. App. LEXIS 33,486 (Fed. Cir. 1991).

The claimed invention must be *identically* disclosed within the four corners of one, and only one, piece of prior art, Scripps Clinic & Research Found. V. Genentech, Inc., 927 F. 2d 1565, 176 (Fed. Cir. 1991). The absence of even a single element from a prior art reference negates anticipation. Atlas Powder Co. v. E. I. Du Pont de Nemours & Co., 750 F. 2d 1569, 1574 (Fed. Cir. 1984).

Applicants Have Met The Standard For Novelty

The pending claims are novel over Au-Young because this reference fails to teach the claimed antibodies that recognize and bind specific portions of the PSCA protein, such as antibodies which bind to amino acids 2-50 (e.g., N-terminal), amino acids 46-109 (e.g., middle portion), or amino acids (85-123) (e.g., C-terminal) of the PSCA protein. Additionally, Au-Young fails to teach embodiments of the antibodies of the invention, including chimeric antibodies, human antibodies, internalizing antibodies, antibody fragments, recombinant proteins having the antigen-binding regions of an anti-PSCA antibody, immunotoxins, immunoconjugates, and hybridomas which produce the antibodies of the invention.

Amended claim 1 recites a monoclonal antibody which binds the N-terminal portion of PSCA consisting of amino acids 2-50 as described in SEQ ID NO:2 (i.e., all or a portion of amino acids 2-50 of the PSCA protein). Amended claim 2 recites a monoclonal antibody which specifically binds the middle portion of PSCA consisting of amino acids 46-109 as described in SEQ ID NO:2 (i.e., all or a portion of amino acids 46-109). Amended claim 3 recites a monoclonal antibody which specifically binds the C-terminal portion of PSCA consisting of amino acids 85-123 as described in SEQ ID NO:2 (i.e., all or a portion of amino acids 85-123).

Au-Young also teaches the predicted amino acid sequence of SCAH (i.e., which is identical to the amino acid sequence of PSCA), but Au-Young was not in possession of the SCAH protein. Further, Au-Young describes producing the SCAH protein in prokaryotic cells such as *E. coli* (see Au-Young at column 27, lines 60-67).

Au-Young prophetically describes making antibodies which bind a SCAH polypeptide. The SCAH protein shares a common amino acid sequence as applicants' PSCA protein. However, Au-Young fails to teach antibodies that bind to a specific portion of the PSCA protein having a specific amino acid sequence, let alone the particular portions of PSCA being claimed.

For example, Au-Young generally teaches producing an antibody using "an amino acid sequence consisting of at least five amino acids, preferably at least 10 amino acids" (column 13, lines 67, and column 14, line 1). However, this description fails to provide guidance to one skilled in the art, because Au-Young fails to specify which particular 5 or 10 amino acid sequence may be used to produce the antibodies. Thus, Au-Young does not specify which portion of the SCAH sequence, having 5 to 10 amino acids, for use in generating antibodies.

Further, Au-Young does not anticipate the claimed invention because Au-Young fails to teach specific portions of the SCAH protein that are likely to be immunogenic for production of antibodies. Au-Young provides no prediction or guidance as to which specific 5 to 10 amino acid sequence could be used as immunogenic peptides for generating anti-SCAH antibodies.

As compared to the elements of the claimed invention, Au-Young fails to teach antibodies that bind to *specific* portions of the PSCA protein, such as amino acids 2-50 (e.g., N-terminal), amino acids 46-109 (middle portion), or amino acids 85-123 (C-terminal). Au-Young fails to teach antibodies that are identical to applicants' antibodies. Au-Young also fails to teach embodiments of the antibodies of the invention. Accordingly, Au-Young does not teach every element of the claimed invention and, therefore, does not anticipate the claimed invention. Withdrawal of this rejection is respectfully requested.

THE REJECTION UNDER 37 U.S.C.§103(a)

In paragraphs 18 and 19 of the Office Action, the Patent Office rejected pending claims 6 and 14, and pending claims 1-5, 9-13, and 15-17, under 35 U.S.C. §103(a). Applicants respectfully traverse the rejections. In rejecting the claims, the Patent Office acted contrary to the guidelines provided by the Federal Circuit as to how to evaluate obviousness with respect to the prior art.

The Standard For Establishing Obviousness Under 35 U.S.C. §103

To establish a prima facie case of obviousness, three basic criteria must be met (MPEP 2143). First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a primary reference or to combine reference teachings. Second, there must be a reasonable expectation of success that the suggested combination will work. Third, the prior art reference (or references when combined) must teach or suggest all of the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicants' disclosure (In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)).

Applicant Has Met The Standard For Non-Obviousness

Applicants have met the legal standard for non-obviousness because none of the cited references, alone or in combination, teach human antibodies or human antibodies conjugated to a cytotoxic agent, that recognize and bind specific portions of the PSCA protein, such as antibodies which bind to a portion consisting of amino acids 2-50 (e.g., N-terminal), a portion consisting of amino acids 46-109 (e.g., middle portion), or a portion consisting of amino acids (85-123) (e.g., C-terminal) of the PSCA protein. Additionally, none of the cited references teach embodiments of the claimed antibodies, including: chimeric antibodies, human antibodies, internalizing antibodies, antibody fragments, recombinant proteins having the antigen-binding regions of an anti-PSCA antibody, immunotoxins, immunoconjugates, and hybridomas which produce the antibodies of the invention.

In paragraph 18 of the Office Action, the Patent Office rejected pending claims 6 and 14 under 35 U.S.C. §103(a) as allegedly unpatentable over Au-Young in view of Green. New claim 20 generally corresponds to claim 6, and new claim 34 generally corresponds to claim 14. Applicants disagree with the rejection for the reasons that follow.

Au-Young has been discussed above. Green does not teach applicants' invention when combined with Au-Young.

Green generally teaches antigen-specific, human, monoclonal antibodies. In particular, Green teaches human monoclonal antibodies directed to tetanus toxin (page 18, first paragraph under the section entitled "Ag-specific fully human mAbs from mice"). However, Green fails to teach or suggest human monoclonal antibodies which bind PSCA.

In summary, Green, alone or in combination with Au-Young, fails to teach human antibodies or human antibodies conjugated to a cytotoxic agent that recognize and bind specific portions of the PSCA protein. Accordingly, there is no motivation to combine the cited references in order to

arrive at the claimed methods. Therefore, the rejection of claims 6 and 14 (e.g., new claims 20 and 34) under 35 U.S.C. §103 is improper and should be withdrawn.

In paragraph 19 of the Office Action, the Patent Office rejected claims 1-5, 9-13, and 15-17 under 35 U.S.C. §103(a) as allegedly unpatentable over Au-Young in view of Thorpe. New claim 22 generally corresponds to claim 4, new claim 18 generally corresponds to claim 6, new claim 23 generally corresponds to claim 9, new claim 25 generally corresponds to claim 10, new claim 24 generally corresponds to claim 11, new claim 34 generally corresponds to claim 12, new claim 34 generally corresponds to claim 13, new claim 29 generally corresponds to claim 15, new claim 29 generally corresponds to claim 16, and new claim 29 generally corresponds to claim 17. Applicants respectfully disagree with the rejection for the reasons that follow.

Au-Young has been discussed above. Green does not overcome the deficiencies of Au-Young. Furthermore, Thorpe does not teach applicants' invention when combined with Au-Young.

Thorpe provides a general review of antibodies conjugated to cytotoxic agents (e.g., immunoconjugates). For example, Thorpe lists particular antibodies conjugated to particular cytotoxic agents, including: anti-human lymphocyte globulin conjugated to diphtheria toxin; anti-Thy 1.1 antibody fragments conjugated to abrin; anti-carcinoembryonic antigen (CEA) antibody conjugated to ricin; anti-T lymphocyte antibody conjugated to ricin; and anti-Thy 1.1 antibody conjugated to gelonin. However, Thorpe fails to teach or suggest antibodies directed to specific portions of PSCA that are conjugated to a cytotoxic agent. Thorpe also fails to teach or suggest anti-PSCA antibodies which are: chimeric antibodies, human antibodies, internalizing antibodies, and antibody fragments thereof.

In summary, Thorpe alone or in combination with Au-Young, fails to teach antibodies directed to specific portions of PSCA that are conjugated to a cytotoxic agent, where the anti-PSCA antibodies are: chimeric antibodies, human antibodies, internalizing antibodies, or antibody fragments. Accordingly, there is no motivation to combine the cited references in order to arrive

at the claimed methods. Therefore, the rejection under 35 U.S.C. §103 is improper and should be withdrawn.

CONCLUSION

Entry of this amendment and the foregoing remarks in the file of the above-captioned patent application is respectfully requested. Applicants believe that all grounds for rejection of the claims have been successfully overcome and that the claims are now in condition for allowance. Withdrawal of the Patent Office's remaining rejections is requested and prompt allowance of the claims is solicited. If any issues remain in connection with the claims, the Examiner is encouraged to contact the undersigned by telephone to discuss the same.

Only the fee for a three-month extension of time is deemed necessary in connection with the filing of this Amendment. The fee for the three-month extension of time is $445.00. A check for $445.00 is enclosed. If any additional fee is necessary, the Patent Office is authorized to charge any additional fee to Deposit Account No. 50-0306.

Pages entitled "Version with Markings to Show Changes in the Title and Specification" and "Version with Markings to Show Changes in the Claims" and "Version with Markings to Show Changes in the Abstract" are attached hereto to show the changes made to the application according to this amendment.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES
IN THE TITLE AND SPECIFICATION

In The Title:

At page 1, line 1, please delete "PSCA: PROSTATE STEM CELL ANTIGEN AND USES THEREOF" and replace with --ANTIBODIES TO PROSTATE STEM CELL ANTIGEN PROTEIN -- .

In The Specification :

At page 1, line 7, please amend this line to read as follows:
-- [08/814,279] 60/228,816, filed March 10, 1997; -- .

At page 6, please delete lines 3-4, "FIG. 1. Nucleotide (A) SEQ ID NO. 1 and translated amino acid (B) SEQ ID NO. 2 sequences of a cDNA encoding human PSCA (ATCC Designation 209612)" and insert the following:
-- **FIG. 1A**. Nucleotide sequence (SEQ ID NO:1, ATCC Designation 209612) of a cDNA encoding human PSCA.

FIG. 1B. Translated amino acid sequence (SEQ ID NO:2) of human PSCA. -- .

At page 6, please delete line 6 "FIG. 2. Nucleotide sequence of a cDNA encoding murine PSCA homologue SEQ ID NO. 3; SEQ ID NO. 4." and insert the following:
--**FIG. 2.** Nucleotide sequence (SEQ ID NO:3), of a murine cDNA PSCA homologue and the translated amino acid sequence (SEQ ID NO:4) of murine PSCA. -- .

At page 6, please amend lines 8-12 to read as follows:

-- **FIG. 3.** Alignment of amino acid sequences of human PSCA (SEQ ID NO:5), murine PSCA (SEQ ID NO:6), and human stem cell antigen-2 (hSCA-2) (SEQ ID NO:7). Shaded regions highlight conserved amino acids. Conserved cysteines are indicated by bold lettering. Four predicted N-glycosylation sites in PSCA are indicated by asterisks. The underlined amino acids at the beginning and end of the protein represent N terminal hydrophobic signal sequences and C terminal GPI-anchoring sequences, respectively [SEQ ID NO. 5; SEQ ID NO. 6; SEQ ID NO. 7]. -- .

At page 6, please delete lines 21-30 "FIG. 7. Restricted Expression of PSCA mRNA in normal and cancerous tissues. **A**: RT-PCR analysis of PSCA expression in normal human tissues demonstrating high expression in prostate, placenta, and tonsils. 1ng of reverse-transcribed first strand cDNA (Clontech, Palo Alto, CA) from the indicated tissues was amplified with PSCA gene specific primers. Data shown are from 30 cycles of amplification. **B**: RT-PCR analysis of PSCA expression demonstrating high level in prostate cancer xenografts and normal tissue. 5ng of reverse-transcribed cDNA from the indicated tissues was amplified with PSCA gene specific primers. Amplification with β-actin gene specific primers demonstrate normalization of the first strand cDNA of the various samples. Data shown are from 25 cycles of amplification. AD, androgen-dependent; AI, androgen-independent; IT, intratibial xenograft; C.L., cell line." and insert the following:

-- **FIG. 7A**. Restricted Expression of PSCA mRNA in normal and cancerous tissues. RT-PCR analysis of PSCA expression in normal human tissues demonstrating high expression in prostate, placenta, and tonsils. 1ng of reverse-transcribed first strand cDNA (Clontech, Palo Alto, CA) from the indicated tissues was amplified with PSCA gene specific primers. Data shown are from 30 cycles of amplification.

FIG. 7B. Restricted Expression of PSCA mRNA in normal and cancerous tissues. RT-PCR analysis of PSCA expression demonstrating high level in prostate cancer xenografts and normal tissue. 5 ng of reverse-transcribed cDNA from the indicated tissues was amplified with PSCA gene

specific primers. Amplification with β-actin gene specific primers demonstrate normalization of the first strand cDNA of the various samples. Data shown are from 25 cycles of amplification. AD, androgen-dependent; AI, androgen-independent; IT, intratibial xenograft; C.L., cell line. -- .

At page 7, please delete lines 2-3 "FIG. 8. Schematic representation of human PSCA, murine PSCA, and human Thy-1/Ly-6 gene structures" and insert the following:
-- **FIG. 8A**. Schematic representation of human Thy-1/Ly-6 gene structures.

FIG. 8B. Schematic representation of murine PSCA gene structure.

FIG. 8C. Schematic representation of human PSCA gene structure. -- .

At page 7, please delete lines 5-10 "FIG. 9. Northern blot analysis of PSCA expression. **A:** Total RNA from normal prostate and LAPC-4 androgen dependent (AD) and independent (AI) prostate cancer xenografts were analyzed using PSCA or PSA specific probes. Equivalent RNA loading and RNA integrity were demonstrated separately by ethidium staining for 18S and 28S RNA. **B:** Human multiple tissue Northern blot analysis of PSCA. The filter was obtained from Clontech (Palo Alto, CA) and contains 2ug of polyA RNA in each lane." and insert the following:
-- **FIG. 9A**. Northern blot analysis of PSCA expression. Total RNA from normal prostate and LAPC-4 androgen dependent (AD) and independent (AI) prostate cancer xenografts were analyzed using PSCA or PSA specific probes. Equivalent RNA loading and RNA integrity were demonstrated separately by ethidium staining for 18S and 28S RNA.

FIG. 9B. Northern blot analysis of PSCA expression. Human multiple tissue Northern blot analysis of PSCA. The filter was obtained from Clontech (Palo Alto, CA) and contains 2ug of polyA RNA in each lane.-- .

At page 7, please delete lines 12-19 "FIG. 10. Northern blot comparison of PSCA, PSMA, and PSA expression in prostate cancer xenografts and tumor cell lines. PSCA and PSMA demonstrate high level prostate cancer specific gene expression. 10 μg of total RNA from the indicated tissues were size fractionated on an agarose/formaldehyde gel, transferred to nitrocellulose, and hybridized sequentially with ^{32}P-labelled probes representing PSCA, PSMA, and PSA cDNA fragments. Shown are 4 hour and 72 hour autoradiogrphic exposures of the membrane and the ethidium bromide gel demonstrating equivalent loading of samples. BPH, benign prostatic hyperplasia; AD, androgen-dependent; AI, androgen-independent; IT, intratibial xenograft; C.L., cell line." and insert the following:

-- **FIG. 10A.** Northern blot analysis of PSCA expression in prostate cancer xenografts and tumor cell lines. PSCA demonstrates high level prostate cancer specific gene expression. 10 μg of total RNA from the indicated tissues were size fractionated on an agarose/formaldehyde gel, transferred to nitrocellulose, and hybridized sequentially with ^{32}P-labelled probes representing PSCA cDNA fragments. Shown are 4 hour and 72 hour autoradiogrphic exposures of the membrane. BPH, benign prostatic hyperplasia; AD, androgen-dependent; AI, androgen-independent; IT, intratibial xenograft; C.L., cell line.

FIG. 10B. Northern blot analysis of PSM expression in prostate cancer xenografts and tumor cell lines. PSM demonstrates high level prostate cancer specific gene expression. 10 μg of total RNA from the indicated tissues were size fractionated on an agarose/formaldehyde gel, transferred to nitrocellulose, and hybridized sequentially with ^{32}P-labelled probes representing PSM cDNA fragments. Shown are 4 hour and 72 hour autoradiogrphic exposures of the membrane. BPH, benign prostatic hyperplasia; AD, androgen-dependent; AI, androgen-independent; IT, intratibial xenograft; C.L., cell line.

FIG. 10C. Northern blot analysis of PSA expression in prostate cancer xenografts and tumor cell lines. 10 μg of total RNA from the indicated tissues were size fractionated on an agarose/formaldehyde gel, transferred to nitrocellulose, and hybridized sequentially with ^{32}P-labelled probes representing PSA cDNA fragments. Shown are 4 hour and 72 hour

autoradiogrphic exposures of the membrane and the ethidium bromide gel demonstrating equivalent loading of samples. BPH, benign prostatic hyperplasia; AD, androgen-dependent; AI, androgen-independent; IT, intratibial xenograft; C.L., cell line. --.

At page 7, please delete lines 21-27 "FIG. 11. In situ hybridization with antisense riboprobe for human PSCA on normal and malignant prostate specimens. **A:** PSCA is expressed by a subset of basal cells within the basal cell epithelium (black arrows), but not by the terminally differentiated secretory cells lining the prostatic ducts (400X magnification). **B:** PSCA is expressed strongly by a high grade prostatic intraepithelial neoplasia (PIN) (black arrow) and by invasive prostate cancer glands (yellow arrows), but is not detectable in normal epithelium (green arrow) at 40X magnification. **C:** Strong expression of PSCA in a case of high grade carcinoma (200X magnification)." and insert the following:
-- **FIG. 11A**. In situ hybridization with antisense riboprobe for human PSCA on normal prostate specimens. PSCA is expressed by a subset of basal cells within the basal cell epithelium (black arrows), but not by the terminally differentiated secretory cells lining the prostatic ducts (400X magnification).

FIG. 11B. In situ hybridization with antisense riboprobe for human PSCA on normal and malignant prostate specimens. PSCA is expressed strongly by a high grade prostatic intraepithelial neoplasia (PIN) (black arrow) and by invasive prostate cancer glands (yellow arrows), but is not detectable in normal epithelium (green arrow) at 40X magnification.

FIG. 11C. In situ hybridization with antisense riboprobe for human PSCA on malignant prostate specimens. Strong expression of PSCA in a case of high grade carcinoma (200X magnification).-- .

At page 7, please delete lines 29-30, and at page 8, please delete lines 1-7 which read as follows: "FIG. 12. Biochemical analysis of PSCA. **A:** PSCA was immunoprecipitated from 293T cells transiently transfected with a PSCA construct and then digested with either N-glycosidase F or O-glycosidase, as described in Materials and Methods. **B:** PSCA was immunoprecipitated from

293T transfected cells, as well as from conditioned media of these cells . Cell-associated PSCA migrates higher than secreted or shed PSCA on a 15% polyacrylamide gel. **C:**FACS analysis of mock-transfected 293T cells, PSCA-transfected 293T cells and LAPC-4 prostate cancer xenograft cells using an affinity purified polyclonal anti-PSCA antibody. Cells were not permeabilized in order to detect only surface expression. The y axis represents relative cell number and the x axis represents fluorescent staining intensity on a logarithmic scale." and insert the following:

-- **FIG. 12A.** Biochemical analysis of PSCA. PSCA was immunoprecipitated from 293T cells transiently transfected with a PSCA construct and then digested with either N-glycosidase F or O-glycosidase, as described in Materials and Methods.

FIG. 12B. Biochemical analysis of PSCA. PSCA was immunoprecipitated from 293T transfected cells, as well as from conditioned media of these cells . Cell-associated PSCA migrates higher than secreted or shed PSCA on a 15% polyacrylamide gel.

FIG 12C. Biochemical analysis of PSCA. FACS analysis of mock-transfected 293T cells, PSCA-transfected 293T cells, and LAPC-4 prostate cancer xenograft cells using an affinity purified polyclonal anti-PSCA antibody. Cells were not permeabilized in order to detect only surface expression. The y axis represents relative cell number and the x axis represents fluorescent staining intensity on a logarithmic scale. -- .

At page 8, please lines 17-20 "FIG. 14. Flow Cytometric analysis of cell surface PSCA expression on prostate cancer xenograft (LAPC-9), prostate cancer cell line (LAPC-4) and normal prostate epithelial cells (PreC) using anti-PSCA monoclonal antibodies 1G8 (green) and 3E6 (red), mouse anti-PSCA polyclonal serum (blue), or control secondary antibody (black). See Example 5 for details." and insert the following:

-- **FIG. 14A.** Flow Cytometric analysis of cell surface PSCA expression on prostate cancer xenograft (LAPC-9) using anti-PSCA monoclonal antibodies 1G8 and 3E6, mouse anti-PSCA polyclonal serum, or control secondary antibody. See Example 5 for details.

FIG. 14B. Flow Cytometric analysis of cell surface PSCA expression on prostate cancer cell line (LAPC-4) using anti-PSCA monoclonal antibodies 1G8 and 3E6, mouse anti-PSCA polyclonal serum, or control secondary antibody. See Example 5 for details.

FIG 14C. Flow Cytometric analysis of cell surface PSCA expression on normal prostate epithelial cells (PreC) using anti-PSCA monoclonal antibodies 1G8 and 3E6, mouse anti-PSCA polyclonal serum, or control secondary antibody. See Example 5 for details. -- .

At page 8, please delete lines 22-24 "FIG. 15. (a) An epitope map for each of the seven disclosed antibodies. (b) Epitope mapping of anti-PSCA monoclonal antibodies conducted by Western blot analysis of GST-PSCA fusion proteins." and insert the following:
-- **FIG. 15A.** An epitope map for each of the seven disclosed antibodies.

FIG 15B. Epitope mapping of anti-PSCA monoclonal antibodies conducted by Western blot analysis of GST-PSCA fusion proteins. -- .

At page 8, please delete line 26 "FIG. 16. A schematic diagram showing that PSCA is a GPI-anchored protein." and insert the following:
-- **FIG. 16A.** Alignment of amino acid sequences of human PSCA, murine PSCA, and human stem cell antigen-2 (hSCA-2). Shaded regions highlight conserved amino acids.

FIG. 16B A schematic diagram showing that PSCA is a GPI-anchored protein. -- .

At page 11, please delete lines 19-24 "Figure 37. A photograph showing immunological reactivity of anti-PSCA mAbs. (A) Immunoprecipitation of PSCA from 293T cells transiently transfected with PSCA using mAbs1G8, 2H9, 3C5, 3E6 and 4A10. The control was an irrelevant murine IgG mAb. (B) Immunoblot analysis of 293T cells transiently transfected with PSCA using the five anti-PSCA mAbs. mAbs 1G8, 3C5 and 4A10 all recognize equivalent molecular forms of PSCA, whereas mAbs 2H9 and 3E6 only weakly recognize deglycosylated forms of PSCA in 293T-PSCA cells in this assay." and insert the following:

-- **FIG. 37.** A photograph showing immunological reactivity of anti-mAbs. Immunoprecipitation of PSCA from 293T cells transiently transfected with PSCA using mAbs 1G8, 2H9, 3C5, 3E6 and 4A10. The control was an irrelevant murine IgG mAb. -- .

At page 12, please delete lines 4-11 "Figure 39. Expression of PSCA in normal tissues. (A) Panel *a* shows staining of bladder transitional epithelium with mAB 1G8. Panel *b* shows colonic neuroendocrine cell staining with mAb 1G8. Double staining with chromogranin confirmed that the positive cells are of neuroendocrine origin (not shown). Panel *c* shows staining of collecting ducts (arrow) and tubules with mAb 3E6. Panel *d* show staining of placental trophoblasts with mAb 3E6. (B) Northern blot analysis of PSCA mRNA expression. Total RNA from normal prostate, kidney, bladder and the LAPC-9 prostate cancer xenograft was analyzed using a PSCA specific probe (top panel). The same membrane was probed with actin to control of loading differences (bottom panel)." and insert the following:

-- **FIG. 39A.** Expression of PSCA in normal tissues. Panel *a* shows staining of bladder transitional epithelium with mAb 1G8. Panel *b* shows colonic neuroendocrine cell staining with mAb 1G8. Double staining with chromogranin confirmed that the positive cells are of neuroendocrine origin (not shown). Panel *c* shows staining of collecting ducts (arrow) and tubules with mAb 3E6. Panel *d* show staining of placental trophoblasts with mAb 3E6.

FIG. 39B. Expression of PSCA in normal tissues. Northern blot analysis of PSCA mRNA expression. Total RNA from normal prostate, kidney, bladder and the LAPC-9 prostate cancer xenograft was analyzed using a PSCA specific probe (top panel). The same membrane was probed with actin to control of loading differences (bottom panel). -- .

At page 12, please delete lines 13-16 "Figure 40. Targeting of mouse PSCA gene. (A) Panel *a* is a schematic drawing showing a strategy for creating a PSCA targeting vector. (B) Panel b is a photograph of a southern blot analysis of genomic DNA using 3' probe showing recovery of wild-type (+/+) and heterozygous (+/-) ES cells." and insert the following:

-- **FIG. 40A.** Targeting of mouse PSCA gene. A schematic drawing showing a strategy for creating a PSCA targeting vector.

FIG. 40B. Targeting of mouse PSCA gene. A photograph of a Southern blot analysis of genomic DNA using 3' probe showing recovery of wild-type (+/+) and heterozygous (+/-) ES cells. -- .

At page 13, please delete lines 7-8 "Photographs of multiple tissue northern blot analysis showing tissue specific expression patterns of human and murine PSCA RNA." and insert the following:

FIG. 47A. Photograph of a multiple tissue Northern blot analysis showing tissue specific expression patterns of human PSCA RNA.

FIG. 47B. Photograph of a multiple tissue Northern blot analysis showing tissue specific expression patterns of murine PSCA RNA. -- .

At page 15, please delete lines 21-22 "FIG. 58. Amino acid sequence of the heavy chain variable domain regions of PSCA monoclonal antibodies 1G8. CDRs are labeled and underlined SEQ ID NO. 10; SEQ ID NO. 11. " and insert the following:

-- **FIG. 58.** Nucleotide sequence (SEQ ID NO:10) and amino acid sequence (SEQ ID NO:11) of the heavy chain variable domain regions of PSCA monoclonal antibodies 1G8. CDRs are labeled and underlined. --.

At page 15, please delete lines 24-25 "FIG. 59. Amino acid sequence of the heavy chain variable domain regions of PSCA monoclonal antibodies 4A10. CDRs are labeled and underlined SEQ ID NO. 12; SEQ ID NO. 13." and insert the following:

-- **FIG. 59.** Nucleotide sequence (SEQ ID NO:12) and amino acid sequence (SEQ ID NO:13) of the heavy chain variable domain regions of PSCA monoclonal antibodies 4A10. CDRs are labeled and underlined. -- .

At page 15, please delete lines 27-28 "FIG. 60. Amino acid sequence of the heavy chain variable domain regions of PSCA monoclonal antibodies 2H9. CDRs are labeled and underlined SEQ ID NO. 14; SEQ ID NO. 15." and insert the following:

FIG. 60. Nucleotide sequence (SEQ ID NO:14) and amino acid sequence (SEQ ID NO:15) of the heavy chain variable domain regions of PSCA monoclonal antibodies 2H9. CDRs are labeled and underlined. -- .

At page 18, please amend lines 1-3 to read as follows:

-- As used herein, PSCA refers to a protein that has the amino acid sequence of human PSCA (SEQ ID NO:2) as provided in FIGS. 1B and 3 [SEQ ID NO. 2; SEQ ID NO. 5; SEQ ID NO. 6; SEQ ID NO. 7], the amino acid sequence of murine PSCA homologue (SEQ ID NO:4) as provided in FIG. 3 [SEQ ID NO. 5; SEQ ID NO. 6. SEQ ID NO. 7], or -- .

At page 18, please amend lines 12-13 to read as follows:

-- The term "PSCA" includes all naturally occurring allelic variants, isoforms, and precursors or human PSCA (SEQ ID NO:2) as provided in FIGS. 1B and 3 [SEQ ID NO. 2; SEQ ID NO. 5; SEQ ID NO. 6; SEQ ID NO. 7] and murine PSCA (SEQ ID NO:4) as provided in FIG. 3 [SEQ ID NO. 5; SEQ ID NO. 6; SEQ ID NO. 7] . -- .

At page 18, please amend lines 13-15 to read as follows:

-- In general, for example, naturally occurring allelic variants of human PSCA will share significant homology (e.g., 70 – 90%) to the PSCA amino acid sequence (SEQ ID NO:2) provided in FIGS. 1B and 3 [SEQ ID NO. 2; SEQ ID NO. 5; SEQ ID NO. 6; SEQ ID NO. 7] . --.

At page 18, please amend lines 22-23 to read as follows:

-- One class of PSCA allelic variants will be proteins that share a high degree of homology with at least a small region of the PSCA amino acid sequences (SEQ ID NOS:2 or 4) presented in FIGS. 1B and 3 [SEQ ID NO. 2; SEQ ID NO. 5; SEQ ID NO. 6; SEQ ID NO. 7] , -- .

At page 19, please amend line 12 to read as follows:

-- The amino acid sequence of human PSCA protein (SEQ ID NO:2) is provided in FIGS. 1B and 3 [SEQ ID NO. 2; SEQ ID NO. 5; SEQ ID NO. 6; SEQ ID NO. 7] . -- .

At page 19, please amend lines 16-17 to read as follows:

-- The amino acid sequence of a murine PSCA homologue (SEQ ID NO:4) is shown in FIG. 3 [SEQ ID NO. 5; SEQ ID NO. 6; SEQ ID NO. 7] . -- .

At page 19, please amend lines 28-29 to read as follows:

-- One example of a functional soluble PSCA protein has the amino acid sequence (SEQ ID NO:2) shown in FIG. 1B [SEQ ID NO. 2] or a fragment thereof. -- .

At page 20, please amend lines 4-5 to read as follows:

-- The invention also provides peptides comprising biologically active fragments of the human (SEQ ID NO:2) and murine (SEQ ID NO:4) PSCA amino acid sequences shown in FIGS. 1B and 3 [SEQ ID NO.2; SEQ ID NO. 5; SEQ ID NO. 6; SEQ ID NO. 7]. -- .

At page 24, line 26-27, please delete "12301 Parklawn Drive, Rockville, MD 20852" and insert the following:

-- 10801 University Boulevard, Manassas, VA 20110-2209. -- .

At page 32, please amend lines 21-22 to read as follows:

-- The nucleotide sequence (SEQ ID NO:1) of a cDNA encoding one allelic form of human PSCA is provided in FIG. 1A [SEQ ID NO.1]. -- .

At page 32, please amend lines 22-23 to read as follows:

-- The nucleotide sequence of a cDNA (SEQ ID NO:3) encoding a murine PSCA homologue ("murine PSCA") is provided in FIG. 2 [SEQ ID NO. 3]. -- .

At page 39, please amend lines 20-21 to read as follows:

-- First, a nucleic acid molecule is obtained that encodes a PSCA protein (SEQ ID NOS:2 or 4) or a fragment thereof, such as the nucleic acid molecule depicted in FIG. 1A [SEQ ID NO. 1]. --.

At page 74, please amend lines 7-9 to read as follows:

-- Clone #15 encodes a 123 amino acid protein (SEQ ID NO:2) which is 30% identical to SCA-2 (SEQ ID NO:5) (also called RIG-E) and contains a number of highly conserved cysteine residues characteristic of the Ly-6/Thy-1 gene family (FIG. 3). -- .

At page 74, please amend lines 17-19 to read as follows:

-- The nucleotide sequence of the full length cDNA (SEQ ID NO:1) encoding human PSCA is shown in FIG. 1A [SEQ ID NO. 1] and the translated amino acid sequence (SEQ ID NO:2) is shown in FIG. 1B [SEQ ID NO. 2] and in FIG. 3 [SEQ ID NO. 5; SEQ ID NO. 6; SEQ ID NO. 7]. -- .

At page 79, please amend lines 22-23 to read as follows:

-- Alignment of these ESTs and 5' extension using RACE-PCR provided the entire coding sequence (SEQ ID NO:4) (FIG. 2) [SEQ ID NO. 3]. -- .

At page 81, please amend lines 12-14 to read as follows:

-- BALB/c mice were immunized three times with a purified PSCA-glutathione S-transferase (GST) fusion protein containing PSCA amino acids 22-99 (SEQ ID NO:2) (FIG. 1B) [SEQ ID NO. 2]. -- .

At page 97, please amend line 7 to read as follows:

-- The PSCA cDNA (SEQ ID NO:1) (Fig. 1) [SEQ ID NO. 1; SEQ ID NO. 2] was used to identify a 130 kb bacterial artificial chromosome (bac) -- .

At page 104, please amend line 24 to read as follows:

-- 5' primer: 5'-TTCTCCTGCTGGCCACCTAC-3' (SEQ ID NO:8) . -- .

At page 104, please amend line 25 to read as follows:

-- 3' primer: 5'-GCAGCTCATCCCTTCACAAT-3' (SEQ ID NO:9) . -- .

At page 106, please amend lines 18-19 to read as follows:

-- Murine monoclonal antibodies were raised against a GST-PSCA fusion protein comprising PSCA amino acid residues 18-98 of the PSCA amino acid sequence (SEQ ID NO:2) (FIG. 1B) [SEQ ID NO. 2] . -- .

At page 118, please amend lines 31-32 to read as follows:

-- The nucleotide (SEQ ID NOS:10, 12, and 14) and amino acid (SEQ ID NOS:11, 13, and 15) sequences are shown in FIGS. 58, 59 and 60, respectively [SEQ ID NO. 10; SEQ ID NO. 11; SEQ ID NO. 12; SEQ ID NO. 13; SEQ ID NO. 14; SEQ ID NO. 15] . -- .

VERSION WITH MARKINGS
TO SHOW CHANGES IN THE CLAIMS

In The Claims:

Please amend claims 1-3. Please cancel claims 4-6 and 9-17 without prejudice to pursue the subject matter of these claims in a continuation application to be filed in the future. Please add new claims 18-35 as follows.

--1. (amended) A monoclonal antibody which recognizes and binds [the] an N-terminal portion of [the] a Prostate Stem Cell Antigen (PSCA) protein [comprising] consisting of amino acids 2 through 50 or a portion thereof as described in SEQ ID NO:2 . --

--2. (amended) A monoclonal antibody which recognizes and binds [the] a middle portion of [the] a Prostate Stem Cell Antigen (PSCA) protein [comprising] consisting of amino acids 46 through 109 or a portion thereof as described in SEQ ID NO:2 . --

--3. (amended) A monoclonal antibody which recognizes and binds [the] a C-terminal portion of [the] a Prostate Stem Cell Antigen (PSCA) protein [comprising] consisting of amino acids 85 through 123 or a portion thereof as described in SEQ ID NO:2. --

--18. (new) The monoclonal antibody of claim 1, 2, or 3 which is a chimeric antibody. --

--19. (new) The monoclonal antibody of claim 4, wherein the chimeric antibody comprises a murine immunoglobulin variable region and a human immunoglobulin constant region. --

--20. (new) The monoclonal antibody of claim 1, 2, or 3 which is a human antibody. --

--21. (new) The monoclonal antibody of claim 6, wherein the human antibody comprises a human immunoglobulin constant region. --

--22. (new) The monoclonal antibody of claim 1, 2, or 3 which is internalized by a cell expressing Prostate Stem Cell Antigen (PSCA). --

--23. (new) A hybridoma which produces the monoclonal antibody of claim 1, 2, or 3. --

--24. (new) A fragment of the monoclonal antibody of claim 1, 2, or 3 which is selected from a group consisting of Fab, F(ab')2, and Fv. --

--25. (new) A recombinant protein comprising the antigen binding region of the monoclonal antibody of claim 1, 2, or 3. --

--26. (new) An immunotoxin comprising the recombinant protein of claim 11 conjugated with a therapeutic agent. --

--27. (new) The immunotoxin of claim 12, wherein the therapeutic agent is a radioactive isotope. --

--28. (new) The immunotoxin of claim 13, wherein the radioisotope is selected from a group consisting of ^{212}Bi, ^{131}I, ^{131}In, ^{90}Y and ^{186}Re. --

--29. (new) The immunotoxin of claim 12, wherein the therapeutic agent is a cytotoxic agent. --

--30. (new) The immunotoxin of claim 15, wherein the cytotoxic agent is selected from a group consisting of ricin, ricin A-chain, doxorubicin, daunorubicin, taxol, ethiduim bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphteria toxin, *Pseudomonas* exotoxin (PE)

A, PE40, abrin, arbrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, and glucocorticoid. --

--31. (new) An immunoconjugate comprising the antibody of claim 1, 2, or 3 conjugated with a therapeutic agent. --

--32. (new) The immunoconjugate of claim 17, wherein the therapeutic agent is a radioactive isotope. --

--33. (new) The immunoconjugate of claim 18, wherein the radioisotope is selected from a group consisting of ^{212}Bi, ^{131}I, ^{131}In, ^{90}Y and ^{186}Re. --

--34. (new) The immunoconjugate of claim 17, wherein the therapeutic agent is a cytotoxic agent. --

--35. (new) The immunotoxin of claim 20, wherein the cytotoxic agent is selected from a group consisting of ricin, ricin A-chain, doxorubicin, daunorubicin, taxol, ethiduim bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphteria toxin, *Pseudomonas* exotoxin (PE) A, PE40, abrin, arbrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, and glucocorticoid. --

VERSION WITH MARKINGS
TO SHOW CHANGES IN THE ABSTRACT

In The Abstract:

At page 129, at lines 5-8, please delete "The invention provides a novel prostate cell-surface antigen, designated Prostate Stem Cell Antigen (PSCA), which is widely over-expressed across all stages of prostate cancer, including high grade prostatic intraepithelial neoplasia (PIN), androgen-dependent and androgen-independent prostate tumors." and insert

-- The invention provides a novel prostate cell-surface antigen, designated Prostate Stem Cell Antigen (PSCA), which is over-expressed across all stages of prostate cancer, bladder cancer, pancreatic cancer, and bone metastasis of prostate cancer. Various embodiments of antibodies specific to PSCA are provided, including antibody fragments, immunoconjugates, internalizing antibodies, chimeric antibodies, human antibodies, and hybridomas which produce the anti-PSCA antibodies -- .